

**REMARKS**

**Introductory Comments:**

Claim 7 was examined in the Office Action under reply and rejected under 35 U.S.C. §112, first and second paragraphs. These rejections are believed to be overcome by the above amendments and are otherwise traversed for reasons discussed below.

**Overview of the Above Amendments and New Claims:**

Claim 7 has been amended to delete the nonelected subject matter, as requested by the Examiner. Nonelected claims 1-6 and 8-26 have been canceled and new claims 27-31 added. The new claims recite particular CD81 sequences and functional equivalents. Support for the new claims can be found in the original claims filed, as well as throughout the specification at, e.g., page 2, line 18 to page 3, line 6; and page 8, lines 3-13.

**Rejection Under 35 U.S.C. §112, Second Paragraph:**

Claim 7 was rejected under 35 U.S.C. §112, second paragraph as indefinite. The Office objects to the alternative statement in the claim which is alleged to encompass a patentably distinct invention. The alternative recitation has been deleted. Thus, this basis for rejection has been overcome.

Additionally, the Office objected to the use of the terminology “functional equivalent” in claim 7, arguing “it is unclear what CD81 equivalent function is being claimed.” Office Action, page 3. Applicant respectfully disagrees. The specification at page 2, lines 21-22 explicitly defines a functional equivalent of CD81 as “a compound which is capable of binding to HCV, preferably to the E2 protein of HCV.” Thus, the claim, when read in light of the specification, as it must be, is clear and definite as written. Thus, this basis for rejection should be withdrawn.

Rejection Based on Lack of Enablement:

The Office rejected claim 7 under 35 U.S.C. §112, first paragraph, for lack of enablement. In particular, the Office states:

The specification does not teach that administration of the CD81 protein or any portion of it, or any compound that in some sense functions the same way as CD81, in fact is of any therapeutic value to a human subject in reducing viral infectivity.

Office Action, page 4 However, applicant respectfully disagrees with these contentions.

In particular, it is well settled that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*Ex parte Forman*, 230 USPQ 546 (P.T.O. Bd. Pat. App. & Int., 1986). Specifically, in order to comply with the enablement requirement of 35 U.S.C. §112, first paragraph, the specification need only set forth such information as is sufficient to allow one of ordinary skill in the art to make and use the invention. How such a teaching is accomplished, either by the use of illustrative examples or by broad terminology, is of no importance since a specification which teaches how to make and use the invention in terms which correspond in scope to the claims must be taken as complying with the first paragraph of §112 unless there is reason to doubt the objective truth of the statements relied upon therein for enabling support (*In re Marzocchi*, 169 USPQ 367 (CCPA 1971)). The burden is on the Office to explain its reasons for the rejection and support the rejection with (i) acceptable evidence, or (ii) reasoning which contradicts the applicant's claim: the reasoning must be supported by current literature as a whole and the Office must prove the disclosure requires undue experimentation. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971). The Office has failed to carry its burden.

Applicant submits that more than adequate information has been provided in order to enable one of skill in the art to make and use the invention. In this regard, an

extensive discussion of methods of making and administering CD81 and functional equivalents thereof as claimed is found in the application, at e.g., pages 5-9 and in the examples. The described methods could readily be used to practice the invention without undue experimentation. The Office is reminded that even a large amount of experimentation is permitted under §112, first paragraph, provided it is routine. *Ex parte Jackson*, 217 USPQ 804, 807 (POBA 1982) (a claim is acceptable under §112 even if it requires extensive experimentation, as long as the experimentation is routine). In light of the disclosure in the application, and in view of the state of the art, applicant submits that the present claims are indeed enabled.

Applicant disagrees with the Office that the specification fails to teach that CD81 is of therapeutic value and that the cited references evidence lack of enablement. To the contrary, Example 5 details the binding of CD81 to recombinant HCV E2. Example 6 demonstrates that the extracellular loop of CD81 binds recombinant E2 and viral particles. Example 7 and Figure 11 show that proteins containing the human EC2 loop of CD81 bound to E2 and inhibited binding of E2 to human cells. Although these data represent results from *in vitro* assays, such assays are traditionally used in the relevant field and are considered indicative of therapeutic efficacy. Thus, one of skill in the art would readily accept applicant's statements in the application regarding efficacy of the claimed invention. For example, page 8, lines 3-7 of the application state:

Since the infection mechanism of HCV appears to depend, in part, upon the availability of a cell surface receptor, making available a soluble form of the CD81 protein, or a functional equivalent thereof will act as an antagonist of binding of HCV to the cellular receptor thus reducing or preventing the infection process and thereby treating the disease.

As explained above, these statements must be accepted by the Office unless there is acceptable reasoning and evidence to dispute them.

The Office has cited Petracca et al. to evidence a lack of therapeutic value of CD81 in treating HCV. However, this reference actually supports applicant's statements regarding therapeutic efficacy. As reported in Petracca et al., CD81 is a cellular receptor for HCV. As explained therein, CD81 binds to HCV E2 with high affinity, analogous to the HIV gp120-CD4 interaction. The Examiner is correct that internalization of ligands by CD81 is inefficient. This does not imply, however, that CD81 is ineffective for treating HCV infection. In fact, the authors propose that CD81 serves as an HCV attachment receptor rather than as a receptor for virus entry and that CD81 may serve to concentrate virus particles at the cell surface for subsequent interaction with an entry receptor. Rice et al., also cited by the Office, explains that multiple receptors or coreceptors are often required for internalization of viruses. See, e.g., page 990, column 2, second full paragraph of Rice et al. Thus, eliminating or reducing the ability of HCV to bind CD81 at the cell surface, e.g., by use of a soluble CD81 which binds circulating HCV, eliminates or reduces the ability of the virus to be internalized and hence the ability of the virus to replicate.

Another factor to be considered in the question of enablement relates to the relative skill of those practicing in the art. Here, the level of ordinary skill in the art of molecular biology and virology is remarkably high. The Office has not identified any methodologies required to practice applicant's invention throughout the scope of the claims, where such methodologies would extend beyond the ability of the routineer. Accordingly, given the level of skill in the art and the extensive disclosure in the application, the claims are believed to be fully enabled.

For all of the foregoing reasons, then, applicant submits that when the relevant enablement factors are actually weighed, as they must be, the balance tips heavily in favor of enablement. The Office's assertion that there is some level of unpredictability in the art does not outweigh the enablement provided by the working examples and detailed guidance supplied by applicant's specification, the state of the art,

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the relative skill of those in the art, and the quantity of experimentation necessary to practice the invention throughout the scope of the claims. Reconsideration and withdrawal of all rejections under 35 U.S.C. §112, first paragraph, is thus respectfully requested.

### CONCLUSION

Applicant respectfully submits that the claims are novel and nonobvious over the art and comply with the requirements of 35 U.S.C. §112. Accordingly, allowance is believed to be in order and an early notification to that effect would be appreciated.

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Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

Claim 7 has been amended as follows:

7. (Amended) A method for treating an infection of HCV comprising administering to a patient a therapeutically effective amount of a CD81 protein, or a functional equivalent thereof [or administering a compound that binds specifically to the CD81 protein], to reduce the infectivity of the virus.

Claims 1-6 and 8-26 have been canceled.

New claims 27-31 have been added:

--27. (New) The method of claim 7, wherein the functional equivalent has at least 80% sequence identity to the human CD81 amino acid sequence depicted in Figure 1.

28. (New) The method of claim 7, wherein the functional equivalent is a soluble form of the CD81 protein.

29. (New) The method of claim 28, wherein the soluble form of the CD81 protein comprises a deletion of one or more of the transmembrane binding domains depicted as TM1, TM2, TM3 and TM4 in Figure 1.

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30. (New) The method of claim 29, wherein the soluble form of the CD81 protein comprises amino acids 113-201 of the human CD81 amino acid sequence depicted in Figure 1.

31. (New) The method of claim 7, wherein the CD81 protein comprises the human CD81 amino acid sequence depicted in Figure 1...  
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